

CLAIMS

1. A preparation comprising a β -amyloid variant or an N-terminal fragment thereof characterized in that said β -amyloid variant or said N-terminal fragment thereof contains an N-terminal truncation and/or a post-translational modification.
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2. The preparation according to claim 1, further characterized in that the N-terminal truncated β -amyloid variant or the N-terminal fragment thereof starts at position 2, 3, 4, 5, 6, 7, 8, 9 or 10 of β -amyloid and that the post-translational modification is a methylation or a pyroglutamylation.
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3. The preparation according to claim 2, further characterized in that the pyroglutamylation is present at position 3 of an N-terminal truncated β -amyloid variant starting at position 3 of β -amyloid.
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4. The preparation according to any of claims 1 to 3, further characterized in that the β -amyloid variant or the N-terminal fragment thereof comprises an amino acid sequence selected from the group consisting of SEQ ID NOs 1 to 165.
- 20 5. The preparation according to any of claims 1 to 4, further characterized in that the β -amyloid variant or the N-terminal fragment thereof contains an additional modification resulting in a separated spot of the β -amyloid variant or the N-terminal fragment thereof on two-dimensional gel electrophoresis compared to the spot obtained with the β -amyloid variant or the N-terminal fragment thereof without said additional modification.
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6. A preparation comprising an N-terminal APP soluble fragment obtainable by secretase cleavage of APP, characterized in that the C-terminal end of said N-terminal APP soluble fragment consists of position 1, 1 to 2, 1 to 3, 1 to 4, 1 to 5, 1 to 6, 1 to 7, 1 to 8, or 1 to 9 of β -amyloid, or a preparation comprising a C-terminal fragment thereof.
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7. The preparation according to claim 6, further characterized in that the N-terminal APP soluble fragment or the C-terminal fragment thereof comprises an amino acid sequence selected from the group consisting of SEQ ID NOs 1 to 6, 14 to 18, 27 to 30, 53 to 55, 66 to 67, 79, and 166 to 261.
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8. A nucleic acid preparation comprising a nucleic acid sequence capable of encoding the β -amyloid variant or the N-terminal fragment thereof according to any of claims 1 to 5.
- 10 9. A nucleic acid preparation comprising a nucleic acid sequence capable of encoding the N-terminal APP soluble fragment or the C-terminal fragment thereof according to any of claims 6 or 7.
- 15 10. A method for the preparation of an antibody that specifically recognizes an N-terminal truncated and/or post-translationally modified β -amyloid variant, comprising the following steps:
- (a) Immunizing an animal with a preparation according to any of claims 1 to 5 or with the nucleic acid preparation according to claim 8;
- (b) Obtaining the antibodies generated by the immunization in step (a);
- 20 (c) Screening the antibodies obtained in step (b) for their specific recognition of N-terminal truncated and/or post-translationally modified β -amyloid variants.
11. An antibody obtainable by the method according to claim 10.
- 25 12. A method for the preparation of an antibody that specifically recognizes an N-terminal APP soluble fragment according to any of claims 6 or 7, comprising the following steps:
- (a) Immunizing an animal with a preparation of N-terminal APP soluble fragment or a C-terminal fragment thereof according to any of claims 6 or 7 or with the
- 30 nucleic acid preparation according to claim 9;
- (b) Obtaining the antibodies generated by the immunization in step (a);
- (c) Screening the antibodies obtained in step (b) for their specific recognition of an N-terminal APP soluble fragment according to any of claims 6 or 7.

13. An antibody obtainable by the method according to claim 12.
14. A vaccine composition or a therapeutic composition comprising a preparation
5 according to any of claims 1 to 5, comprising an antibody according to claim 11,
or comprising a nucleic acid preparation according to claim 8.
15. A preparation according to any of claims 1 to 5, an antibody according to claim
11, or a nucleic acid preparation according to claim 8 for use as a prophylactic
10 vaccine for the prevention of a disease associated with β -amyloid formation
and/or aggregation such as Alzheimer's disease.
16. A preparation according to any of claims 1 to 5, an antibody according to claim
11, or a nucleic acid preparation according to claim 8 for use as a therapeutic for
15 the treatment of a disease associated with β -amyloid formation and/or aggregation
such as Alzheimer's disease.
17. Use of a preparation according to any of claims 1 to 5, an antibody according to
claim 11, or a nucleic acid preparation according to claim 8 for the manufacture of
20 a prophylactic vaccine for the prevention of a disease associated with β -amyloid
formation and/or aggregation such as Alzheimer's disease.
18. Use of a preparation according to any of claims 1 to 5, an antibody according to
claim 11, or a nucleic acid preparation according to claim 8 for the manufacture of
25 a therapeutic for the treatment of a disease associated with β -amyloid formation
and/or aggregation such as Alzheimer's disease.
19. A method for the prevention and/or treatment, in a mammal, of a disease
associated with β -amyloid formation and/or aggregation such as Alzheimer's
30 disease, said method comprising the administration, to said mammal, of a vaccine
composition or a therapeutic composition according to claim 14.

20. A diagnostic or theranostic kit comprising a preparation according to any of claims 1 to 5, comprising a preparation according to any of claims 6 or 7, or comprising an antibody according to any of claims 11 or 13.
- 5 21. A preparation according to any of claims 1 to 5 for use as a diagnostic or theranostic for the measurement of the immune response induced in a mammal by vaccination or therapeutic application with respectively a vaccine composition or a therapeutic composition according to claim 14.
- 10 22. Use of a preparation according to any of claims 1 to 5 for the manufacture of a diagnostic or theranostic kit for the measurement of the immune response induced in a mammal by vaccination or therapeutic application with respectively a vaccine composition or a therapeutic composition according to claim 14.
- 15 23. A method for the measurement, in a mammal, of the immune response induced by vaccination or therapeutic application with respectively a vaccine composition or a therapeutic composition according to claim 14, said method comprising the following steps:
- 20 (a) Determining, in a sample obtained from said mammal, the amount of antibody specific for a β -amyloid variant according to any of claims 1 to 5;
- (b) Comparing the amount determined in step (a) with the amount of antibody specific for said β -amyloid variant present in the mammal before vaccination or therapeutic application with the vaccine or therapeutic composition according to claim 14;
- 25 (c) Concluding, from the comparison in step (b), whether the mammal is responding to the vaccination or therapy, an increased amount of antibody specific for said β -amyloid variant being an indication that the mammal is responding to the vaccination or therapy.
- 30 24. A preparation according to any of claims 1 to 5, an antibody according to claim 11 or 13, or a preparation according to any of claims 6 or 7 for use as a diagnostic or theranostic for determining, in a mammal, the susceptibility to a disease associated with β -amyloid formation and/or aggregation such as Alzheimer's disease, for

determining, in a mammal, the risk of developing a disease associated with β -amyloid formation and/or aggregation such as Alzheimer's disease, for screening of the clearance of β -amyloid deposition in a mammal, or for predicting the level of β -amyloid burden in a mammal.

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25. Use of a preparation according to any of claims 1 to 5, an antibody according to claim 11 or 13, or a preparation according to any of claims 6 or 7 for the manufacture of a diagnostic or theranostic kit for determining, in a mammal, the susceptibility to a disease associated with β -amyloid formation and/or aggregation
10 such as Alzheimer's disease, for determining, in a mammal, the risk of developing a disease associated with β -amyloid formation and/or aggregation such as Alzheimer's disease, for screening of the clearance of β -amyloid deposition in a mammal, or for predicting the level of β -amyloid burden in a mammal.

15 26. A method for determining, in a mammal, the susceptibility to a disease associated with β -amyloid formation and/or aggregation such as Alzheimer's disease, for determining, in a mammal, the risk of developing a disease associated with β -amyloid formation and/or aggregation such as Alzheimer's disease, for screening of the clearance of β -amyloid deposition in a mammal, or for predicting the level
20 of β -amyloid burden in a mammal, said method comprising the following steps:

- (a) Determining, in said mammal, the amount of β -amyloid variant according to any of claims 1 to 5, the amount of N-terminal APP soluble fragment according to any of claims 6 or 7, or the amount of antibody specific for said β -amyloid variant or said APP soluble fragment;
- 25 (b) Comparing the amount determined in step (a) with the amount of said β -amyloid variant, said N-terminal APP soluble fragment, or said antibody in a control mammal;
- (c) Concluding, from the comparison in step (b), whether the mammal is susceptible to a disease associated with β -amyloid formation and/or
30 aggregation such as Alzheimer's disease, whether the mammal is at risk of developing a disease associated with β -amyloid formation and/or aggregation

such as Alzheimer's disease, whether the β -amyloid deposition in the mammal is cleared, or what the level of β -amyloid burden is in said mammal.

27. The method according to claim 26, further characterized in that the amount of β -amyloid variant, the amount of N-terminal APP soluble fragment or the amount of antibody specific for said β -amyloid variant or said N-terminal APP soluble fragment is determined on a tissue sample obtained from said mammal.
28. The method according to claim 27 for predicting the level of β -amyloid burden in a mammal, said method comprising the following steps:
- (a) Administration, to said mammal, of a vaccine composition or a therapeutic composition according to claim 14;
 - (b) Determining, in a biological fluid sample obtained from said mammal, the amount of β -amyloid variant according to any of claims 1 to 5;
 - (c) Comparing the amount determined in step (b) with the amount of said β -amyloid variant in a biological fluid sample obtained from a control mammal;
 - (d) Concluding, from the comparison in step (c), what the level of β -amyloid burden is in said mammal.